Parameter Analysis and Refinement Toolkit System and its Application in MM3 Parameterization for Phosphine and its Derivatives

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ABSTRACT

The multiparameter multistep relaxation (MPMSR) method, a routine within a new suite of parameterization programs entitled *parameter analysis and refinement toolkit system* (PARTS), was developed to assist in the development of molecular mechanics (MM3 and MM2) force field parameters and represents an ongoing effort in our laboratories to generate more accurate force fields in shorter times. In contrast to other computerized parameterization approaches, this method simulates intuition guided trial-and-error and has been used successfully within our laboratories to develop MM2 and MM3 force fields. The primary aim of this approach is to minimize human inspection time and effort, with simultaneous improvement in the efficiency and accuracy of the parameterization process. In an effort to validate the generality of the MPMSR method, a well parameterized data set of phosphine derivatives was reexamined. With the identical set of training molecules used in the original MM3 phosphine parameterization and with minimal human intervention, MPMSR shortened the process from several months to approximately five days. Although the previous phosphine force field is well parameterized, the newly generated MPMSR set of parameters has achieved an overall better fit to the experimentally observed data and *ab initio* calculations.

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Introduction

Molecular mechanics is a computational method that is routinely used by chemists to predict the molecular geometry, conformations, and energies for many classes of organic compounds. The accuracy of molecular mechanics calculations often rivals experiment; however, all the parameters for each unique combination of atoms must be rigorously determined and incorporated into the program. The reliability of these calculations is greatly dependent on the transferable parameters.[1] Transferability means that the force constant parameters may be used within the same force field for different molecules that have similar structures. However, it will not give accurate results if parameters are transferred from one program to another. In general, there is an art and a science to molecular mechanics parameterization. At one extreme, least-squares fitting methods have been used to optimize the parameters to the best fit between the calculated and experimental data.[2-4] At the other extreme, parameters may be determined by inspection on an intuition guided trial-and-error basis.[5]

Least-squares fitting routines have been applied to molecular mechanics parameterization. With modern computers, it has become more efficient and economical to utilize their inherent power for molecular mechanics parameterization. Some serious problems arise, nevertheless, if standard least-squares methods are indiscriminately used. For example, if MM3 vibrational frequencies are to be compared with experimental spectral data, many complex potential energy functions regarding the frequency calculations are necessary. In practice, people tend to use simplified models to avoid these intensive calculations. These simplifications introduce errors into the parameterization process. Even if all the complex functions are included, there are still other potentially serious problems.

First, force field parameters are highly coupled with the calculated geometry of the molecules in the training set. Any calculated property (i.e., dipole moment or vibrational frequency) is dependent on both the final optimized geometry and the specific force field parameters. At the same time, the final optimized geometry is a function of the force field parameters included. It is essentially impossible to set up a direct mathematical relationship among the starting geometry, final optimized geometry, and force field parameters without going through a geometry optimization routine. This relationship produces an interesting cycle: Molecular mechanics parameterization is dependent on the correct final geometry that, in turn, is dependent on the correct parameters, ... When a least-squares fitting program needs geometry information to do further calculations (i.e., first derivatives of each force field parameter), the starting geometry is often used as a final optimized geometry. Even if the starting geometry has been previously optimized, the final geometry will change when the force field parameters are altered during parameterization. If the starting geometry is used to do all the calculations, the cycle is broken, but it also can introduce simultaneously large deviations.

Second, molecular mechanics is essentially an empirical method. The parameters in the force field are not a complete set of orthogonal variables in mathematics, which is a requisite of most least-squares fitting routines. There is a strong correlation, as indicated above, among the molecular mechanics force field parameters, and it is very difficult to describe this correlation mathematically. If some errors or arbitrary decisions are introduced regarding a single parameter, the effect is usually transferred throughout the force field. In other words, the remaining parameters in the force field must be altered to compensate for the errors previously introduced.[6] In some cases, one can even develop two or more sets of parameters that can reproduce experimental data equally well,[7] although one of them may be closer to the chemist's conception of the system. This situation cannot be handled adequately by simple least-squares fitting routines.

Mathematically, the overall root-mean-square (rms) deviation of a particular training molecule containing m atoms can be expressed as

$$\text{rms} = f(P_1, P_2, P_3, \ldots, P_n, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m) \quad (1)$$

where $P_1, P_2, P_3, \ldots, P_n$ are all force field parameters required for the molecular mechanics calculation of this molecule and $x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m$ are the optimized Cartesian

coordinates of this training molecule. Then

$$\frac{\partial(\text{rms})}{\partial P_1} = \left(\frac{\partial(\text{rms})}{\partial P_1}\right)_{P_2, P_3, \ldots, P_n, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} + \left(\frac{\partial(\text{rms})}{\partial P_2}\right)_{P_1, P_3, \ldots, P_n, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} \cdot \frac{\partial(P_2)}{\partial P_1} + \left(\frac{\partial(\text{rms})}{\partial P_3}\right)_{P_1, P_2, \ldots, P_n, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} \cdot \frac{\partial(P_3)}{\partial P_1} + \cdots + \cdots + \left(\frac{\partial(\text{rms})}{\partial P_n}\right)_{P_1, P_2, P_3, \ldots, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} \cdot \frac{\partial(P_n)}{\partial P_1} + \left(\frac{\partial(\text{rms})}{\partial x_1}\right)_{P_1, P_2, P_3, \ldots, P_n, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} \cdot \frac{\partial(x_1)}{\partial P_1} + \left(\frac{\partial(\text{rms})}{\partial y_1}\right)_{P_1, P_2, P_3, \ldots, P_n, x_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m, z_m} \cdot \frac{\partial(y_1)}{\partial P_1} + \cdots + \cdots + \left(\frac{\partial(\text{rms})}{\partial z_m}\right)_{P_1, P_2, P_3, \ldots, P_n, x_1, y_1, z_1, x_2, y_2, z_2, \ldots, x_m, y_m} \cdot \frac{\partial(z_m)}{\partial P_1} \quad (2)$$

However, in the molecular mechanics force field, $\partial(P_2)/\partial P_1$, $\partial(P_3)/\partial P_1, \ldots,$ $\partial(P_n)/\partial P_1$, $\partial(x_1)/\partial P_1$, $\partial(y_1)/\partial P_1, \ldots,$ and $\partial(z_m)/\partial P_1$ cannot be described analytically, and they are too difficult and time intensive to be calculated numerically on a routine basis. In most cases, these terms are ignored, and the equation of the derivative is truncated after the first term. In the molecular mechanics force field, $\partial(P_2)/\partial P_1$, $\partial(P_3)/\partial P_1, \ldots,$ $\partial(P_n)/\partial P_1$ describe the correlation between the force field parameters, and $\partial(x_1)/\partial P_1$, $\partial(y_1)/\partial P_1, \ldots, \partial(z_m)/\partial P_1$ represent the correlation between the geometric variables of a training set of molecules and the force field parameters. Truncating these terms from the equation of the first derivative of the root-mean-square deviation simply means that these correlations are excluded from consideration by the least-squares fitting method.

Finally, it is difficult for a computerized least-squares fitting method to evaluate the overall performance of a set of molecular mechanics force field parameters. During the parameterization, the criteria used to evaluate the force field are the deviations between the calculated results and experimental (and/or *ab initio*) data. The major criteria include the deviations of bond lengths, bond angles, torsion angles, dipole moments, moments of inertia, and vibrational frequencies. These criteria, however, are not equally important for all kinds of parameters. For example, the deviations of bond lengths are more important than those of bond angles and vibrational frequencies for the development of equilibrium bond length parameters and, consequently, they should be weighted more heavily. Likewise, the deviations of vibrational frequencies should be given greater priority than other deviations during the optimization of stretching and bending force constants. During molecular mechanics parameterization, the set of training molecules should be as large as practical. The contributions of each training molecule often need to be weighted differently. A molecule with more reliable experimental data should be ranked higher in priority than other structures for which the experimental data are equivocal. Even for the same molecule, various subsets of the data may be more reliable than others. During molecular mechanics parameterization, all these factors should be considered to correctly evaluate the performance of a set of force field parameters. Because there is no general rule to merge all these factors into one final performance index, the evaluation of a set of force field parameters requires extensive parameterization experience and is difficult to carry out consistently unaided by specialized computer programs. The least-squares fitting method may eliminate small local random errors but introduce large systematic errors. Therefore, the results

generated by this method should be examined carefully.

The trial-and-error method, where one alters a single parameter at a time, usually leads to better overall results, but it is extremely time intensive and requires intimate knowledge of the chemical structures of the molecules in the training set. It typically takes many months, and perhaps even years, to generate one set of highly accurate parameters. Although a significant amount of time is spent on judging the reliability of the experimental data, it still takes considerable time to adjust the parameters to minimize the deviations between calculation and experiment. Large systematic errors usually can be eliminated through the chemist's intuition in the trial-and-error inspection approach; however, due to human limitations, small random errors still remain. In contrast to both least-squares fitting and trial-and-error methods, our approach with multiparameter multistep relaxation (MPMSR) combines the chemical intuition with modern computational power to reduce systematic and random errors. The final results are better molecular mechanics force field parameters in significantly less time.

Mechanism of Multiparameter Multistep Relaxation Method

In essence the MPMSR method simulates the intuition-guided trial-and-error approach described above. The accuracy of molecular mechanics calculations is dependent upon the equations comprising the force field as well as the parameters or constants found in the equations. Theoretically, there is an optimum set of parameters that fit both experimental data and chemical intuition. Each parameter in this optimum set is at its ideal value. A molecular mechanics force field with this optimum parameter set may be referred to as a *balanced* system. If a parameter in a molecular mechanics force field is not correct, the performance of this force field decreases, and this system is referred to as an *unbalanced* system. Because the parameters in the molecular mechanics force field mathematically are not a complete set of orthogonal variables, there are strong correlations among all these parameters, i.e., they are highly coupled. If for whatever reason one parameter deviates from its ideal value (*balanced* position), the remaining parameters will be perturbed. The first parameter that is inaccurate (the original reason causing the force field to be out of balance) will generate what is referred to as an unbalancing force. It is this unbalancing force that shifts the force field into an overall unbalanced state. What the MPMSR method attempts to do is to relax (or minimize) this unbalancing force and to restore the unbalanced molecular mechanics force field.

Molecular mechanics parameters may be divided into two categories. The first set of parameters are those that have been determined previously and should not be altered—*fixed* parameters. The second set of parameters are those that need to be optimized in the current parameterization—*trial* parameters. In any set of trial parameters, there is generally more than one constant (multiparameter) that must be assigned a value. Each of these constants can be optimized by MPMSR individually, while others are kept constant. In most cases, especially at the beginning of a new parameterization work, many unbalancing forces exist, and the force field is far from its balanced position. For multiparameter evaluations, MPMSR needs to scan the entire trial parameter set and relax all of the unbalancing forces. After MPMSR has optimized all trial parameters once, the first parameter is no longer at its "best" value and MPMSR must then reoptimize it (multistep). This process can be repeated iteratively, so that the unbalancing forces on all parameters can be gradually relaxed until the system is balanced.

To determine the state of success in the parameterization, MPMSR calculates a final performance index from the deviations of bond lengths, bond angles, torsion angles, dipole moments, and vibrational frequencies. The weighting factors for each of these deviations are assigned by the user. The effect of one deviation on the parameterization can be eliminated by assigning a zero weighting factor to it. These weighting factors are very important in determining the final values of the force field parameters. Different weighting factors can lead the parameterization through different optimization paths and achieve different optimized parameter sets. It is the chemist's responsibility to use reasonable weighting factors under different circumstances so that the final parameters make sense chemically. In addition to the final optimized parameters, MPMSR also saves all deviations of all molecules in the training set for further examination.

In applications of MM3 parameterization, after the torsional parameters have been determined through either torsional energy profiles and/or vibrational frequencies (strongly attributed by the corresponding torsional modes), users need to adjust parameters for bond lengths, bond angles, stretching force constants, bending force constants, out-of-plane bending constants, bond moments, and electronegativities. The first iteration normally starts with parameters that have the least coupling, for example, bond lengths and bond angles. Using the experimentally determined data (neutron diffraction or X-ray) or *ab initio* generated molecular geometry as templates, MPMSR can quickly optimize equilibrium bond length and bond angle parameters by assigning a higher weight to geometrical deviations. In order to create more transferable force fields and decrease random errors, a large set of diverse training structures should be used. Nevertheless, for many reasons, some data are more reliable than others. MPMSR can take the quality of data into account by weighting training molecules individually.

The next group of parameters that needs to be determined during force field development is the stretching force constants, bending force constants, and out-of-plane bending force constants. Initially, we normally give greater weight to vibrational frequencies for the development of force constant parameters. When MM3 vibrational frequencies are compared to those obtained by experimental or *ab initio* methods, it is important to make sure that identical vibrational modes are compared correctly with each other. If *ab initio* calculated frequencies are used, the original (*ab initio* calculated) eigenvector matrix or replacement matrix can be used to match the corresponding MM3 calculated matrix. If an experimental spectrum is used, one has to manually determine which MM3 mode corresponds to which experimental assignment. Once the assignments are accomplished, MPMSR can lock into those modes even if the numerical order of frequencies has changed. It is noteworthy that ingredients of some empirically calculated vibrational modes are dependent on the values of force field parameters. This is especially true for the modes that include skeleton deformations. To overcome this difficulty, MPMSR reports identities (the cross product of replacement vectors for two modes is currently used as the mode identity) between MM3 vibrational modes and their corresponding experimental/*ab initio* modes. Manual reassignments may be necessary to ensure correct mode matching if one observes a mode identity that is too low after several cycles of MPMSR.

Since bond moment parameters do not couple with other parameters extensively, they can also be determined approximately in the first trial run. Clearly, overall dipole moments are major criteria for optimization of bond moment parameters. In contrast, electronegativity parameters have complicated coupling patterns with the rest of the force field, especially with equilibrium bond lengths and bond stretching force constant parameters. Therefore, electronegativities are not included in the first trial run. The purpose of the first trial is to find a relatively reasonable starting point so that convergence may be achieved more readily in the later fine tuning optimization stages. This process can be repeated several times to further push the force field parameters closer to the ideal balanced values. During these early approximation runs, the process can be controlled interactively by adjusting different weighting factors.

The parameters generated from the first trial should be able to reproduce most of the molecular properties with reasonably small deviations. Adding electronegativity parameters can further increase the accuracy by taking into account subtle chemical environments caused by neighboring atoms. Since the electronegativity parameters affect both bond lengths and stretching force constants, they must be optimized together with according weighting factors for both bond length and vibrational frequencies (they can be weighted equally at the beginning). Since these parameters couple with one another extensively, MPMSR repeats this process until they all reach the converging criteria or the maximum number of cycles.

The fine tuning stage is aimed at making final adjustments to all parameters while ensuring the best possible results. During this phase, all parameters are included and all force field performance criteria are weighted accordingly (again, they can be weighted equally if no preference is given to any of them). MPMSR monitors the overall performance of the force field while adjusting each of the parameters on a small scale so that they can converge individually. After all parameters are optimized once, MPMSR goes back to check whether the current values are still the best fitting ones for each parameter to ensure the overall convergence of the entire force field.

Application of the MPMSR to Alkylphosphine Parameters

MPMSR was developed during the MM3 parameterization of oxocarbenium ions (unpublished research report; MM2 parameters were developed in the same laboratory[8]). To make sure the program was working properly and providing accurate results for general molecular mechanics parameterization, it was decided to test the MPMSR method by repeating one of our previous parameterization projects and comparing the results with the parameters derived from the trial-and-error inspection method. One carefully developed parameter set, alkylphosphines, was selected for the

TABLE I.
The MM3(MPMSR) and MM3(94) Parameter Sets for Alkylphospines.[a]

Bond stretching parameters

Bond	l_0 (Å)	k_s
P–H [b]	1.4370 (1.420)	3.080 (3.065)
P–C	1.8394 (1.843)	2.890 (2.940)

Angle bending parameters

Atoms	k_q	q_0 (degrees)		
		type 1	type 2	type 3
H–P–H	0.700 (0.680)	91.95 (92.2)	93.50 (93.5)	c
C–P–H	0.640 (0.705)	94.80 (94.7)	95.65 (96.4)	c
C–P–C	0.750 (0.770)	96.75 (95.6)	97.25 (98.1)	c
P–C–H	0.600 (0.570)	107.80 (111:0)	107.50 (108.4)	108.40 (108.6)
P–C–C	0.700 (0.600)	112.15 (107.5)	106.80 (109.6)	109.00 (108.0)

Torsional parameters

Atom types	V_1	V_2	V_3
H–P–C–H	0.000 (0.000)	0.000 (0.000)	0.290 (0.290)
C–P–C–H	0.000 (0.000)	0.000 (0.000)	0.410 (0.410)
H–P–C–C	–0.447 (–0.447)	–2.612 (–2.612)	0.560 (0.560)
P–C–C–H	0.000 (0.000)	0.000 (0.000)	0.305 (0.305)
C–P–C–C	–1.430 (–1.430)	0.000 (0.000)	0.589 (0.589)

Electronegativity correction parameters

Atom types defining bond	End of bond	Attached Atom	Correction to l_0
C–P	C	C	+0.0000 (+0.0025)
C–P	C	H	–0.0010 (+0.0000)
C–P	P	C	+0.0040 (+0.0000)
C–P	P	H	+0.0105 (+0.0070)
P–H	P	C	–0.0135 (+0.0000)
C–C	C	P	+0.0015 (+0.0000)
C–H	C	P	–0.0010 (–0.0030)

Torsion – Stretch parameter

Atoms defining Bond	k_{tb}
C–P	0.000 (0.1040)

Dipole parameters

Atoms defining bond	Bond Moment
C–P	0.949 (+0.81)
H–P	0.523 (–0.53)

[a] These parameters were generated by MPMSR based on MM3(94). The numbers in parentheses are parameters from the original study (rep. 9).
[b] P = atom type 25, C = atom type 1, and H = atom type 5 in MM3.
[c] For angles with atom type 25 as the central atom, no MM3 type 3 bend constants are possible.

comparison test.[9] Using the same experimental data, the parameterization was restarted *de novo*. The MPMSR parameterization was completed within five days compared to the months required using the trial-and-error inspection approach. As shown in Table I, these two parameter sets are very similar, and they both make sense chemically. The only difference is that in addition to eliminating the large systematic error, which was also done through the trial-and-error inspection approach, the MPMSR method further reduces small random errors and finely tunes the parameters more accurately. Since MPMSR is mainly used for molecular mechanics nontorsional parameters, the original trial-and-error torsional parameters were not reexamined.

It is noteworthy to point out that in the original MM3 phosphine parameterization, the C—P and H—P bond moment vectors were defined in opposite directions. This led to the correct orientation of the dipole moment vector for trimethylphosphine, but the incorrect orientation for phosphine. In the MPMSR work, more accurate C—P and H—P bond moments were selected to correct for this problem. Now the correct magnitude and orientation for the dipole moments are calculated with the new MPMSR parameters.

PHOSPHINE

The electron diffraction structure of phosphine has been reported by Bartell and Hirst.[10] The vibrational frequencies of phosphine are also known experimentally.[11] Table II shows the experimental structural data and the MM3 results. In this table, MM3 refers to molecular geometry calculated using the existing parameters developed by the trial-and-error inspection approach previously reported.[9] The second MM3 calculation, MM3(MPMSR), used the parameters derived from the MPMSR method. Phosphine is the only compound in the training set which has a ∠H—P—H bond angle, and it is trivial to fit this bond angle without any deviation. In contrast, since the equilibrium P—H bond length parameter affects more than one molecule, it should be adjusted to the best value for all molecules. The best deviation given by the trial-and-error method is 0.017 Å, and the MPMSR method gives 0.000 Å. Comparing the vibrational frequencies between the results of these two methods (Table III), one can see the root-mean-square deviation from the trial-and-error method is 37 cm^{-1}, while that from the MPMSR method is 35 cm^{-1}. For phosphine, MPMSR improves the performance of the molecular mechanics force field for both the molecular geometry and vibrational frequencies.

METHYLPHOSPHINE

The bond lengths, bond angles, and vibrational frequencies for methylphosphine are shown in Tables IV[12,13] and V.[14] Comparing the performance of the old parameter set derived by the trial-and-error method and the new one generated by MPMSR, the deviations of bond lengths and bond angles are similar. In the vibrational frequency simulation, the parameters from the MPMSR method reproduce the experimental results much better than the trial-and-error parameters. The root-mean-square deviation for vibrational frequencies is improved from 45 to 36 cm^{-1}. In Table V, it can be seen that four vibrational modes have large deviations in the trial-and-error parameter set, e.g., the two CH_3 wag modes have deviations of 97 and 60 cm^{-1} and the PH_2 twist and PH_2 wag modes have deviations of 118 and 45 cm^{-1}, respectively. Using the new parameter set from the MPMSR method, the deviations of these four vibrational modes are reduced to 85, 46, 87, and 11 cm^{-1}, respectively.

TABLE II.
Structure of Phosphine.

	ED[a]	MM3[b]	Deviation	MM3(MPMSR)[c]	Deviation
P–H	1.437±0.004	1.420	–0.017	1.437	0.0
∠ H–P–H	93.5	93.5	0.0	93.5	0.0

[a] Experimental data from ref. 9.
[b] MM3 results with the parameters reported in ref. 8.
[c] MM3 results with the parameters generated through the MPMSR approach.

TABLE III.
Vibrational Modes of Phosphine.

Assignment	Expll [a]	MM3[b]	Deviation	MM3(MPMSR)[c]	Deviation
P-H asym str	2328	2309	-19	2315.1	-12.9
P-H asym str	2328	2309	-19	2315.1	-12.9
P-H sym str	2323	2303	-20	2308.7	-14.3
P-H asym bnd	1122	1092	-30	1094.8	-27.2
P-H asym bnd	1122	1092	-30	1094.8	-27.2
P-H sym bnd	992	1064	72	1066.3	74.3
		rms	37	rms	35.4

[a]Experimental data from ref. 10.
[b]MM3 results with the parameters reported in ref. 8.
[c]MM3 results with the parameters generated through the MPMSR approach.

TABLE IV.
Structure of Methylphosphine.

	ED or MW[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–H	1.423(7)	1.4205	-0.003	1.424	0.0010
P–C	1.858(3)	1.8574	<-0.001	1.8567	-0.0013
C–H (average)	1.094(8)	1.1089	0.015	1.1109	0.0170
∠ P–C–H	109.6(10)	110.16	0.6	110.041	0.441
∠ H–P–H	[93.38]	92.75	-0.63	92.502	-0.878
∠ C–P–H	[97.50]	97.06	-0.44	96.432	-1.068
∠ H–C–H (average)	[109.75]	108.77	-0.96	108.934	-0.816

[a]Electron diffraction data from ref. 11. The number inside the square bracket is microwave data from ref. 12.

TABLE V.
Vibrational Assignment for Methylphosphine.

Assignment	Symm	IR Gas[a]	MM3	Deviat.	MM3(MPMSR)	Deviat.
C-H asym str	A"	3003	3014	11	2993.6	-9.2
C-H asym str	A'	2990	3012	22	2992.1	2.3
C-H sym str	A'	2936	2908	28	2888.5	-47.9
P-H asym str	A"	2309	2305	-4	2310.4	1.4
P-H sym str	A'	2305	2302	-3	2307.9	3.3
CH_3 Asym bnd	A'	1435	1422	-14	1418.8	-16.4
CH_3 Asym bnd	A"	1429	1419	-10	1415.7	-12.9
CH_3 sym bnd	A'	1296	1286	-10	1294.6	-1.6
PH_2 Sciss	A'	1092	1085	-7	1095.0	3.1
CH_3 wag	A"	1017	920	-97	932.4	-84.5
CH_3 wag	A'	978	917	-60	931.3	-46.3
PH_2 twist	A"	(696)	814	118	782.7	86.8
PH_2 wag	A'	730	775	45	740.4	10.9
C-P stretch	A'	676	685	9	684.1	8.4
int. torsion	A"	219	212	-8	212.1	-6.9
			rms	45	rms	36.4

[a]All the experimental IR values are from ref. 13. The value in parentheses is from the solid phase data reported in the same reference.

TABLE VI.
Structure of Dimethylphosphine.

	ED/WM[a]	MM3	Deviation[b]	MM3(MPMSR)	Deviation[b]
P–H	(1.418)[d]	1.4205	0.0025	1.4155	-0.0025
P–C	1.853±0.003	1.8529	–0.0001	1.8528	-0.0002
C–H (average)	1.097±0.007	1.1088	0.0118	1.1107	0.0137
∠ C–P–H	(96.5)[c]	96.2	-0.3	96.495	-0.005
∠ P–C–H (average)	109.8±0.7	110.2	0.4	110.082	0.282
∠ C–P–C	99.2±0.6	99.8	0.6	99.211	0.011

[a]The electron diffraction data and the microwave data are both taken from refs. 8 and 11.
[b]In all the tables the deviation of the difference between the calculated MM3 value and the electron diffraction data is shown where available. If no ED data are available for a particular structural feature, the microwave data are used.
[c]The C — P — H angle value is an assumed value.
[d]Because of the extreme length of the P — H bond (angstroms) determined by electron diffraction, this microwave value was used in the data analysis.

DIMETHYLPHOSPHINE

As shown in Table VI, the MPMSR parameters give almost the same deviations for P—H and P—C bond lengths as the trial-and-error parameters. The deviations using both sets of parameters are within the experimental accuracy. Using the previously reported trial-and-error parameters, MM3 reproduces the C—H bond length better than using the MPMSR parameters with devia-

TABLE VII.
Vibrational Assignments of Dimethylphosphine.

Assignments	sym	IR Gas	MM3	Dev.	MM3(MPMSR)	Dev.
C-H(A') asymm .str.	A'	2985	3014	29	2994.5	9.5
C-H (A')sym str.	A'	2975	3014	29	2994.2	19.2
C-H(A") asymm str.	A"	2985	3014	39	2994.1	9.1
C-H(A") asymm str.	A"	2975	3013	38	2993.0	18.0
C-H (A") sym str.	A'	2923	2909	-14	2889.7	-33.3
C-H (A') sym str.	A"	2918	2909	-9	2889.6	-28.4
P-H Stretch (A')	A'	2288	2304	16	2310.4	22.4
(A')C-H3 asym def.	A'	1447	1429	-18	1426.7	-20.3
(A")C-H3 asym def.	A"	1443	1425	-18	1421.9	-21.1
(A')C-H3 asym def.	A'	1434	1423	-12	1419.2	-14.8
(A")C-H3 asym def.	A"	1434	1421	-14	1417.3	-16.7
(A')C-H3 sym def.	A'	1297	1290	-7	1298.3	1.3
(A")C-H3 sym def.	A"	1284	1288	4	1296.2	12.2
(A")P-H bnd + CH3 rock(22%)	A"	1012	927	-85	943.5	-68.5
(A') CH3 rock	A'	990	927	-63	937.1	-52.9
(A")C-H3 rock +P-C str(11%)	A'	986	921	-65	930.0	-56.0
(A")C-H3 rock +P-C str(21%)	A"	954	909	-45	924.5	-29.5
(A') CH3 rock	A"	947	870	-77	834.1	-103.9
(A')P-H bnd +C-P str(16%)	A'	729	718	-11	697.8	-31.2
(A") P-C asym str	A"	703	699	-4	689.2	-13.8
(A')P-C asym str+C-P-C def(13%)	A'	660	663	3	665.0	5.0
(A') C-P-C def	A'	261	264	3	261.2	0.2
CH3 torsion	A'	190.7	199	9	201.0	10.3
CH3 torsion	A"	188.8	178	-11	179.1	-9.7
			rms	35	rms	34.4

tions of 0.012 and 0.014 Å for trial-and-error parameters and MPMSR parameters, respectively. The new parameters improve all bond angles for dimethylphosphine. The bond angle deviations are decreased from 0.3 to 0.0 for ∠C—P—H, from 0.4 to 0.3 for ∠P—C—H, and from 0.6 to 0.0 for ∠C—P—P. The MPMSR parameters and trial-and-error parameters give similar root-mean-square deviations in the frequency calculations: 34 cm^{-1} for the MPMSR parameters and 35 cm^{-1} for the trial-and-error parameters (Table VII). Overall for dimethylphosphine, both parameter sets reproduce the experimental results very well.

TRIMETHYLPHOSPHINE

As shown in Table VIII, the MPMSR parameters yield a better result for the P—C bond length, while the trial-and-error parameters reproduce the C—H bond lengths and bond angles better. Both sets of parameters reproduce the vibrational frequencies very well. As shown in Table IX, the root-mean-square deviations of vibrational frequencies using the trial-and-error parameters and MPMSR parameters are 22 and 17 cm^{-1}, respectively.[15,16] Trimethylphosphine has three "silent" vibrational modes with A2 symmetry. These vibrational modes cannot be observed in either infrared or Raman spectroscopy, so they could not be compared with the calculated frequencies. The only exception is the torsional A2 vibrational mode with frequency of 223 cm^{-1}. The vibrational frequency of this torsional A2 mode was determined via microwave spectroscopy.[17]

ETHYLPHOSPHINE

Durig and co-workers have reported the structure of the *gauche* and *trans* conformers of ethylphosphine by studying a number of isotopically substituted species using microwave spectroscopy.[18] They have determined that ethylphosphine exists in a *trans/gauche* ratio of 55:45. The new MPMSR parameters and the old trial-and-error parameters yield similar deviations for bond lengths and bond angles. The bond length deviations using the MPMSR parameter set are about 0.001–0.002 Å smaller than the corresponding ones using the previously reported parameter set for *gauche*-ethylphosphine, and about the same for the *trans*-ethylphosphine. The bond angle deviations from MPMSR parameters are smaller for the *trans* conformer and larger for the *gauche* conformer than the ones from the comparison parameter set. They both vary within a range of 0.6°. The calculated vibrational frequencies of both *gauche*- and *trans*-ethylphosphine have been compared to the experimental data (Tables X and XI). The MPMSR parameter set further reduces the root-mean-square deviation of the *trans* conformation from 36 to 32 cm^{-1} and from 35 to 34 cm^{-1} for the *gauche* conformation (data not shown).

GAUCHE-ISOPROPYLPHOSPHINE

Both parameter sets reproduce the experimental geometry (see Table XII) for *gauche*-isopropylphosphine very well.[19] The MPMSR parameter set improves the P—H bond length by 0.005 Å and the C—C bond length by 0.002 Å, while the P—C bond length is 0.004 Å worse. Compared to the bond angles calculated using the trial-and-error parameters, the new parameter set further reduces the deviation of the ∠H—P—H and ∠C—C—C bond angles by about 0.2 and 1.0°, respectively, while the ∠C—C—P and ∠C—P—H bond angles have no significant change. The root-mean-square deviation of vibrational frequencies is 37 cm^{-1} using the old parameter set and 35 cm^{-1} for the new parameter set (data not shown).

ETHYLDIMETHYLPHOSPHINE

Ethyldimethylphosphine also has been studied by Durig and co-workers.[20,21] For the reasons outlined in the original parameterization report,[9] neither the new MPMSR parameter set nor the trial-and-error parameter set can fit *trans*-ethyldimethylphosphine very well, especially the C—C bond length and the C—C—P bond angle. The MPMSR parameter set gives better bond length fitting to both *gauche* and *trans* conformers, while

TABLE VIII.
Structure of Trimethylphosphine.

	ED	MM3	Deviation	MM3(MPMSR)	Deviation
P–C	1.846±0.003	1.8456	-0.0004	1.8459	-0.0001
C–H (average)	1.091±0.006	1.1086	0.0176	1.1106	0.0196
∠ P–C–H	110.7±0.5	110.3	-0.4	110.126	-0.574
∠ C–P–C	98.6±0.3	98.6	0.0	99.602	1.002

TABLE IX.
Vibrational Assignment for Trimethylphosphine.

Assignment	Symm	Gas IR[a]	MM3	Dev	MM3(MPMSR)	Dev
CH_3 asym. str.	A1	2988	3017	29	2996.6	8.6
CH_3 asym. str.	E	2978	3016	38	2995.7	17.7
CH_3 asym. str.	E	2978	3016	38	2995.7	17.7
CH_3 asym. str.	E	2968	3014	46	2994.6	26.6
CH_3 asym. str.	E	2968	3014	46	2994.6	26.6
CH_3 asym. str.	A2		3013		2993.7	
CH_3 sym. str.	A1	2900	2911	-4	2891.1	-8.9
CH_3 sym. str.	E	2900	2911	11	2890.9	-9.1
CH_3 sym. str.	E	2890	2911	21	2890.9	0.9
CH_3 asym. bnd.	A1	1441	1435	-6	1430.8	-10.2
CH_3 asym. bnd.	E	1430	1431	1	1426.6	-3.4
CH_3 asym. bnd.	E	1430	1431	1	1426.6	-3.4
CH_3 asym. bnd.	E	1416	1428	12	1423.5	7.5
CH_3 asym. bnd.	E	1416	1428	12	1423.5	7.5
CH_3 asym. bnd.	A2		1424		1419.9	
CH_3 sym. bnd.	A1	1312	1298	-14	1302.6	-9.4
CH_3 sym. bnd.	E	1297	1294	-4	1299.0	2.0
CH_3 sym. bnd.	E	1283	1294	11	1299.0	16.0
CH_3 Wag	A1	(973)	942	-31	957.0	-16.0
CH_3 Wag	E	952	927	-13	943.2	-8.8
CH_3 Wag	E	952	927	-13	943.2	-8.8
P-C-H bnd	E	940	908	-27	924.0	-16.0
P-C-H bnd	E	940	908	-27	924.0	-16.0
CH_3 Wag	A2		901		917.5	
P-C asym str	E	709	697	-12	697.0	-12.0
P-C asym str	E	706	697	-9	697.0	-9.0
P-C sym str	A1	(653)	647	-6	643.8	-9.2
C-P-C sym bnd	A1	(305)	272	-33	264.7	-40.3
C-P-C asym bnd	E	(263)	262	-1	259.9	-3.1
C-P-C asym bnd	E	(263)	262	-1	259.9	-3.1
CH_3 twist	E	248	217	-31	217.1	-30.9
CH_3 twist	E	248	217	-31	217.1	-30.9
CH_3 twist	A2	223 [b]	192	-5	194.1	-28.9
			rms	22	rms	16.9

[a] Experimental data from refs. 14 and 15.
[b] This "silent" vibrational mode was calculated from the microwave spectrum in ref. 16.

TABLE X.
Structures of *trans*-Ethylphosphine.

	MW[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–H	1.4230	1.4200	-0.0030	1.4180	-0.0050
P–C	1.8465	1.8642	0.0177	1.8628	0.0163
C–C	1.5334	1.5332	-0.0002	1.5346	0.0012
∠ H–P–H	92.89	94.61	1.72	94.301	1.411
∠ C–P–H	96.31	97.71	1.40	97.108	0.798
∠ C–C–P	116.31	112.36	-3.95	112.892	-3.418
∠ P–C–H	106.68	108.37	1.69	107.748	1.068

[a] Experimental data from ref. 17.

TABLE XI.
Structures of gauche-Ethylphosphine.

	MW[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–H	1.4153	1.4205	0.0052	1.4185	0.0032
	1.4169	1.4205	0.0036	1.4185	0.0016
P–C	1.8525	1.8646	0.0121	1.8629	0.0104
C–C	1.5355	1.5325	-0.0030	1.5338	-0.0017
∠ H–P–H	92.68	92.18	-0.50	91.949	-0.731
∠ C–P–H	97.86	97.03	-0.82	96.424	-1.436
	96.75	97.00	0.25	96.422	-0.328
∠ C–C–P	110.65	110.90	0.25	111.562	0.912
∠ P–C–H	111.48	109.23	-2.25	108.610	-2.870
	106.93	108.55	1.62	107.887	0.957

[a]Experimental data from ref. 17.

the bond angle fitting is essentially the same for these two sets of parameters, displayed in Tables XIII and XIV. Comparing the vibrational frequencies, the new parameter set gives a smaller root-mean-square deviation to the *trans* conformer and larger deviation for the *gauche* conformer within the range of 0.9 cm^{-1} (data not shown).

TERT-BUTYLPHOSPHINE

The bond lengths and the bond angles calculated using both sets of parameters, shown in Table XV, have been compared to the experimental results.[22] Comparing the MM3 calculated bond lengths to the experimental data, the new MPMSR parameters give better results for the P—C and P—H bond lengths, while the calculations using the trial-and-error parameters have a smaller deviation for the C—C bond length. Also, the MPMSR parameter set improves the ∠C—C—C and ∠C—P—H bond angles by 1.4 and 0.8°, respectively, while it makes the ∠H—P—H bond angle 0.2° worse than the old parameter set. The old error-and-trial parameters fit the vibrational frequency to the root-mean-square deviation of 35 cm^{-1}, while the new MPMSR parameters further reduce the root-mean-square deviation to 30 cm^{-1} (data not shown).

Conclusions

The multiparameter multistep relaxation (MPMSR) method has been developed and demonstrated to be a useful tool for molecular

TABLE XII.
Structure of *gauche*-Isopropylphosphine.[a]

	MW[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–C	1.878	1.8758	-0.0022	1.8720	-0.0060
P–H [b]	1.414	1.4199[c]	0.0059	1.4145	0.0005
C–C [d]	1.527	1.5382	0.0112	1.5373	0.0103
C–C–P	109.5	109.7[c]	0.2	109.479	-0.021
H–P–H[b]	93.4	94.1	0.7	93.892	0.492
C–P–H[b]	97.5	97.7	0.2	97.268	-0.231
C–C–C[d]	111.8	110.5	-1.3	111.503	-0.297

[a]Structure taken from ref. 18.
[b]Experimental value assumed to be the same as in methylphosphine.
[c]Value expressed as the average of two unequal values.
[d]Experimental value assumed to be the same as in isopropylamine.

TABLE XIII.
Structures of *gauche*-Ethyldimethylphosphine.

	ED[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–C [b]	1.848	1.8490	0.0010	1.8482	0.0002
C–C	1.559	1.5330	–0.0260	1.5343	-0.0247
∠ Me–P–Et	99.6	99.1	-0.5	100.107	-1.393
∠ Me–P–Me	101.5	98.5	-3.0	99.479	-2.021
∠ C–C–P	112.3	111.7	–0.6	112.253	-0.047
∠ P–C–H[c]	110.5	110.3	–0.2	110.178	-0.322

[a]Experimental data from ref. 19.
[b]Average value for all P — C bond lengths.
[c]Only the angles of the P — CH_3 are considered in this measurement.

TABLE XIV.
Structures of *trans*-Ethyldimethylphosphine.

	ED[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P–C [b]	1.848	1.8472	-0.0008	1.8482	0.0002
C–C	1.559	1.5328	-0.0262	1.5343	-0.0247
∠ Me–P–Et	99.6	101.9	2.3	102.686	3.086
∠ Me–P–Me	101.5	99.5	-2.0	100.401	-1.099
∠ C–C–P	107.6	116.5	8.9	116.142	8.542
∠ P–C–H[c]	110.5	110.4	-0.1	110.217	-0.283

[a]Experimental data from ref. 21.
[b]Average value for all P — C bond lengths.
[c]Only the angles of the P — CH_3 are considered in this measurement.

TABLE XV.
Structure of *t*-Butylphosphine.

	MW[a]	MM3	Deviation	MM3(MPMSR)	Deviation
P-C	1.896	1.8825	-0.0135	1.886	-0.0100
C-C fixed	1.535	1.5396	0.0046	1.5450	0.0100
P-H fixed	1.414	1.4198	0.0058	1.4124	-0.0016
@PMe3					
∠C-C-C fixed	108.5	110.0	1.5	108.417	-0.083
∠H-P-H Fixed	93.4	93.3	–0.1	93.103	-0.297
∠C-P-H	95.7	97.7	2.0	96.913	1.213

[a]The microwave structural data are taken from ref. 22.

mechanics parameterization. It combines the chemist's intuition and the computer's speed to incorporate advantages from both the trial-and-error and the least-squares fitting methods. In contrast to the least-squares method, the MPMSR approach gives users more control over the parameterization, so the resulting parameter set makes more sense chemically. Compared to the traditional trial-and-error method, MPMSR greatly reduces the human labor involved in parameterization and decreases the overall deviation attributable to random errors.

In summary, the MPMSR method is a combined approach of intuition-guided and least-squares parameterization methods. The intuition-guided method is used to establish an overall working plan, e.g., which parameter(s) should be optimized and in what order, as well as what criteria should

be used to evaluate the performance of each parameter and with what weighting factors. Additionally, the intuition-guided method is also used to monitor the progress of the parameterization and intervene if necessary to ensure that the process is going along a "correct" (chemically reasonable) optimization path. On the other hand, the least-squares method is used to handle all the optimizations for every parameter under the direct control of user's intuition.

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